ROLES OF THE EXTRACELLULAR MACROMOLECULES IN DEVELOPMENT OF THE CENTRAL NERVOUS SYSTEM

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Summary

One the major component of the extracellular matrix (ECM) is hyaluronan (HA) that is important for organization of other ECM molecules and in the regulation of cell-matrix communication.

We investigated the expression pattern of HA and HA-binding chondroitin-sulphate proteoglycans (CSPG) in spinal cord of chicken embryos in order that providing new data about the possible roles of these molecules in differentiating neurons and axon guidance and sprouting. Using biotynilated HA specific binding complex (bHABC) combined with immunofluorescent labeling of differentiating neurons in histological sections of spinal cords, HA was surrounding around neuroprogenitor cells before their postmitotic stage. These finding suggested the non-permissive role of HA in neuroprogenitor cell proliferation but it was possible that permissive for differentiation. We showed by RT-PCR two hyaluronan synthases HAS2 and 3 expressed by the developing spinal cord in each stages indicating that these molecules were producing HA and they might also were functioning as a HA receptor binding it the to the cell surface. By using RT-PCR and histotechnique, we also found a set of HA-binding CSPGs (lecticans) expressed by embryonic spinal cord. The expression pattern of these lecticans were largely overlapped with the HA reaction suggesting a functional relationship between the lecticans and HA to form HA-lectican complexes. Among lecticans the neurocan was expressed in earlier stage of development while the highly glycosylated lectican (aggrecan) was expressed by older embryos. Increasing of the relative amount of chondroitin-sulphate during differentiation of the spinal cord suggests that both chondroitin-sulphate and core protein has functional role in embryonic development. Another CSPG, phosphacan also were expressed by developing spinal cord. We found that phosphacan was accumulating around proliferating neurons and in the peripheral nerves and in their entry zone as well as in the white matter. Interestingly the axons in the grey matter did not contain phosphacan.

In the second part of our work we found changes in distribution of HA after transsection of the vestibulocochlear nerve in frogs. During regeneration HA decreased in the vestibular nuclei that received the primary afferents, including structural changes in the perineuronal net. These findings suggest a non-permissive role of HA to the axon sprouting in the central nervous system while the HA might be permissive in the peripheral nerves which indicated by the finding of increased HA relative amount during regeneration.

Keywords: Extracellular matrix, Neuronal development, Image analysis, Neural regeneration